

QUALITY OF LIFE IN PATIENTS WITH HYPOTHYROIDISM AND HYPERTHYROIDISM

Ján BIELIK^{1*} – Emília SLÁVIKOVÁ² – Vladimír MELUŠ¹ – Matej BIELIK³

¹ Faculty of Healthcare, Alexander Dubček University of Trenčín, Študentská 2, 911 50 Trenčín, Slovak Republic

² Faculty Hospital Trenčín, Legionárska 28, 911 71 Trenčín, Slovakia

³ Endocrinology Out-patient department, Nové Mesto nad Váhom, Slovakia

*Corresponding author E-mail address: jan.bielik@tnuni.sk

Abstract

Background: Quality of life obtained from patients' data is becoming a significant part of treatment efficiency evaluation. Up until now, there was not a study dedicated to QoL in patients with hypothyroidism and hyperthyroidism in Slovakia.

Methods: To find out the Quality of Life (QoL) in this study, an original QoL questionnaire developed by Faculty of Health, Alexander Dubček university in Trenčín (FoH TnUAD) was used. The questionnaire is predominantly generic, and oriented towards work ability (WA) as well as QoL. The results were processed using basic statistical methods included in Excel 2013 software, while to determine statistically significant differences of the parameters compared Dunn's, Friedman's and Mann-Whitney's tests were used.

Results: When evaluating the whole set, the current quality of life was at 7.8, at the time of diagnosing the disease it was 5.8, at the time of disease - 8.2, and finally in the time of full health, the quality of life reached 9.0 (1- worst, 10- best). In the group of patients with hyperthyroidism compared to the group of patients with hypothyroidism, results were: 6.4 vs. 7.3; 4.6 vs. 6.0; 7.6 vs. 8.3; 8.0 vs. 9.2. The average treatment time was 11.3 years. The mean duration of the symptoms before the diagnosis was 0.9 years. Patients visited an endocrinologist due to the disease 2.7 times a year and their general practitioner for an average of 3.4 times a year. Patients also evaluated their own personality, which can determine the perception of overall quality of life, ranging from 1 (pessimistic) to 5 (optimistic). The assessment of the expectations for the future was as follows: (1- worst, 5- best): health expectations 3.6; economical - 3.4; working - 3.6. Family expectations reached the highest rating - 4.2. Patients evaluated their disease awareness on a 5-point scale at 4.3, provided medical care 4.7, and nursing care 4.7 (1- worst, 5- best).

Conclusions: Quality of life varies significantly at the time of diagnosis and in treatment, both in hypothyroidism and hyperthyroidism. Quality of life is significantly worse at the time of diagnosis in hyperthyroidism. Drugs (Thyrozol, Propycil) have no significant effect on the quality of life in the treatment of hyperthyroidism. Drugs (Euthyrox, L-Thyroxine BCH) have no significant effect on the quality of life in the treatment of hypothyroidism. The quality of life in patients with total strumectomy or unilateral lobectomy does not differ from patients with hypothyroidism and hyperthyroidism.

Key words: Quality of life. Hypothyroidism. Hyperthyroidism.

1 Introduction

Autoimmune thyroiditis (AIT) is the most common thyroid disease and the most common thyroiditis in Slovakia and other countries with normalized iodine intake even after the decline of the endemic goiter. Women are more than 10 times more likely to be sick than men. AIT affects up to 4% of adolescents and young women, with its prevalence increasing in correlation with age [1]. In the geriatric population of women its prevalence is estimated at 15-20%. In the general population, autoantibodies against thyroid antigen were found in 10% of women [2, 3]. Hypothyroidism occurs in 3-10% of adult patients, with elderly women having an incidence that is higher [4-6]. Hyperthyroidism, most commonly represented by Graves' disease, is the most common form of hyperthyroidism, with a prevalence of about 0.5% in males and about 3.0% in females [7]. Clinical signs, especially in the case of a developed disease, have a significant impact on the sense of health. In the case of hyperthyroidism, it can be unrest, hurry, heat dissipation, perspiration, palpitations, muscle weakness, insomnia, tendency to diarrhea, weight loss, endocrine orbitopathy - pressure sensations, vision disorder [8]. In the case of hypothyroidism, it may be total fatigue, somnolence, feeling cold, slowing down of mental and physical activities, constipation, flatulence, skin itching, skin dryness, soreness of the skin with pressure, especially eyes [8].

2 Quality of life

Quality of life (QoL) is the subject of several definitions. In practice, subjective assessment of personality disposition for satisfaction in life, especially for self and secondary for relatives and loved ones, is expressed (ideally) in numerical value. QoL examined in relation to health is referred to as HRQoL (Health Related QoL) [9]. For the assessment of quality of life, original or generic questionnaires, which are often strictly patient-based, are used. In that case it is PROS - patients reported outcomes [10]. The method allows for the comparison of clinical effect of the treatment, as well as its economic value. The evaluation of the quality of life can also be reflected in healthcare or drug policy [11].

3 Methods

The quality of life questionnaire developed by the Faculty of Healthcare, Alexander Dubček University in Trenčín (FZ TnUAD) was used in this study to determine the quality of life. The questionnaire is predominantly generic in nature and is focused on quality of life (QoL) as well as on the work ability (WA). The results were processed by the basic statistical methods included in Excel 2013, while the following tests were used to determine the statistically significant differences in the comparison parameters: Dunn test, Friedman test and Mann-Whitney test.

4 Results

4.1 The sample file

The group comprised a total of 213 patients, of whom 180 were hypothyroidism patients and 33 hyperthyroidism patients. The mean age of patients was 53.4 years. There were 35 male patients with an average age of 53.0 years. There were 178 women with an average age of 53.4 years. The marital status was: single - 39, married and widowed - 121, widows and widowers - 22, divorced - 15 and living in the same household - 6 (10 patients did not fill in this category). 28 patients had primary education, secondary education - 142 patients, and university education - 40 patients (3 patients did not fill in this category). The average treatment time was 11.3 years. The mean duration of the symptoms before diagnosis was 0.9 years. The thyroid character was as follows: 144 diffuse thyroid gland, the nodule goiter - 21, and the thyroid gland - 48. Totally 8 patients underwent strumectomy, 2 patients unilateral lobectomy and 203 patients had no thyroid surgery. A total of 164 patients were on Euthyrox at a mean dose of 76.8 µg /day, L-Thyroxine BCH - 15 patients at an average dose of 79.5 µg /day, Thyrozol - 24 patients at an average dose of 14.4 mg /day and Propycil used 7 patients at an average dose of 207.1 µg /day.

4.2 Quality of life

Quality of life was evaluated on a numerical scale from 0 to 10, while 0 represented the worst quality of life, and 10 the best quality of life. To measure the impact of the disease itself on the quality of life, patients also evaluated quality of life before the disease, and to filter any other comorbid conditions patients evaluated quality of life in so-called full health. Current quality of life allowed the evaluation of impact of treatment on quality of life. The results as well as basic statistical data are in table 1.

Table 1 Quality of life in hypothyroidism and hyperthyroidism

Disease	QoL	n	\bar{x}	sd	x_m	min.	max.
Hyperthyroidism	Current	33	6.4	2.3	7	0	10
	In time of diagnosis	33	4.6	2.8	5	0	10
	Without disease	33	7.6	1.6	8	4	10
	Full health	33	8.0	1.9	9	1	10
Hypothyroidism	Current	180	7.3	1.9	8	1	10
	In time of diagnosis	179	6.0	2.4	6	0	10
	Without disease	176	8.3	1.6	8	2	10
	Full health	178	9.2	1.2	9	1	10

In verifying the differences in quality of life in all four phases, Friedman's test showed statistically extremely significant differences (Table 2, $p < 0.001$). Therefore, Dunn's test was then performed between pairs of phases. Dunn's test revealed statistically significant differences between the current quality of life and overall health ($p < 0.001$), QoL at time of diagnosis and QoL at time without disease ($p < 0.001$) as well as between QoL at the time of diagnosis and QoL at full health ($p < 0.001$). The results are shown in Table 2.

Table 2 Quality of life in hyperthyroidism in relation to time according to Friedman and Dunn's tests

Hyperthyroidism	n	x_m	p	Dunn's test				
				Hyperthyroidism	Current	In time of diagnosis	Without disease	Full health
Current	33	7	<0.001	Current		ns	ns	***
In time of diagnosis	33	5		In time of diagnosis	ns		***	***
Without disease	33	8		Without disease	ns	***		ns
Full health	33	9		Full health	***	***	ns	

Legend: p- Friedman's test value criterion, ns- non significant, ***- $p < 0.001$

In the case of testing quality of life results in patients with hyperthyroidism, differences in quality of life were statistically significant at each phase, both in the case of Friedman’s total test and Dunn’s test of individual pairs. The results are shown in Table 3.

Table 3 Quality of life in hypothyroidism in relation to time evaluated by Friedman’s and Dunn’s test

Hypothyroidism	n*	x _m	p	Dunn’s test				
				Hypothyroidism	Current	In time of diagnosis	Without disease	Full health
Current	175	8	<0.001	Current		**	***	***
In time of diagnosis	175	6		In time of diagnosis	**		***	***
Without disease	175	8		Without disease	***	***		***
Full health	175	9		Full health	***	***	***	

Legend: p- Friedman’s test value criterion, * number was adjusted to the par-form of the test, respondents with missing data were eliminated from the test; ns- non-significant, *** - p<0.001.

In assessing differences in quality of life between hyperthyroidism and hyperthyroidism, statistically significant differences were observed between time of disease, time without disease and time of full health, but not at the present time, i.e. during treatment. The results are shown in Table 4.

Table 4 Comparison of QoL between patient files depending on the time period

QoL	Sample file	n	\bar{x}	sd	x _m	min.	max.	p
Current	Hyperthyroidism	33	6.4	2.3	7	0	33	0.06
	Hypothyroidism	180	7.3	1.9	8	1	10	
In time of diagnosis	Hyperthyroidism	33	4.6	2.8	5	0	10	0.007
	Hypothyroidism	179	6.0	2.4	6	0	10	
Without disease	Hyperthyroidism	33	7.6	1.6	8	4	10	0.02
	Hypothyroidism	176	8.3	1.6	8	2	10	
Full health	Hyperthyroidism	33	8.0	1.9	9	1	10	<0.001
	Hypothyroidism	178	9.2	1.2	9	1	10	

Legend: p- Mann-Whitney’s test value criterion

As there were no differences found in current quality of life in hypo- and hyperthyroidism, the following evaluations compared the parameters of the whole sample file to the quality of life. In the evaluation, current quality of life was 7,8, in time of diagnosis – 5.8, without disease – 8.2 and in full health – 9.0.

The patients also evaluated their personality, which can determine their experience of quality of life, on the scale from 1 (pessimist) to 5 (optimist). The average value was 3.7, so the patients evaluated themselves as optimistic in personality at about 74%.

This was also reflected in the evaluation of future expectations (1-worst, 5- best): medical – 3.6; economical – 3.4; working – 3.6. Familial expectations reached the highest values – 4.2.

Patients visited an endocrinologist due to their disease 2.7-times a year, and their general practitioner about 3.4-times a year.

Patients evaluated their knowledgeability about the disease on a 5-point numeric scale as 4.3, provided medical care – 4.7 and nursing care – 4.7 (1-worst, 5- best).

Average disability with thyroidism was minimal at 1.5 day/year (in disabled group), in other diseases up to 59.9 days/year. Drugs cost per year was minimal – 2.7 €, other medical care related costs (other than transport) – 1€, and transport cost – 4.5 €. Hypothetical Willingness to pay for full recovery was 49.0 €m which was 10.63% of an average monthly income – 460.8 €.

Type of drug does not have any significant impact on quality of life in hypo- or hyperthyroidism, as found evaluating the relation between type of treatment and quality of life. The results are shown in Tables 5 and 6.

Table 5 Quality of life in hyperthyroidism by kind of pharmacotherapy

QoL/Drug	n	\bar{x}	sd	x _m	min.	max.	p
Thyrozol	22	6.4	2.2	7	0	9	0.65
Propycil	7	6.9	2.3	8	3	10	

Legend: p- Mann-Whitney’s test value criterion

Tabuľka 6 Quality of life in hypothyroidism by kind of pharmacotherapy

QoL/Drug	n	\bar{x}	sd	x _m	min.	max.	p
Euthyrox	163	7.2	2.0	8	1	10	0.18
L-Thyroxin	14	7.9	1.5	8	5	10	

Legend: p- Mann-Whitney’s test value criterion

Other aspects/parameters were examined in relation to quality of life on the basis of correlation. Positive correlation to quality of life was found in the case of “positive” familial, working, economical and medical expectations, as well as higher education and optimistic personality in hypothyroidism. Medical and nursing care positively correlate with quality of life in both hypo- and hyperthyroidism. There was no correlation between marital status, duration of the disease, duration of the symptoms, number of endocrinologist visits, knowledgeable about disease and willingness to pay. Correlations are shown in table 7.

Table 7 Correlations of quality of life and other parameters in hypo- and hyperthyroidism

Quality of life in relation to parameters	Hypothyroidism			Hyperthyroidism		
	n	R	p	n	R	p
Education	178	0.18	0.02	32	0.23	0.20
Personality	173	0.22	0.002	32	0.05	0.80
Marital status*	173	0.00	0.99	31	0.19	0.29
Expectations medical	179	0.47	<0.001	33	0.07	0.70
Expectations economical	175	0.38	<0.001	33	0.18	0.32
Expectations working	157	0.37	<0.001	32	0.07	0.70
Expectations familial	174	0.22	0.004	33	0.21	0.24
Duration of disease	173	0.00	0.98	33	0.00	0.98
Duration of symptoms	165	-0.02	0.81	30	0.20	0.28
Endocrinologist visits	180	-0.03	0.65	33	0.13	0.48
Knowledgeability	179	0.13	0.09	33	0.30	0.09
Medical care	178	0.19	0.01	33	0.42	0.02
Nursing care	178	0.21	0.004	33	0.42	0.02
Willingness to pay	150	0.02	0.77	27	-0.13	0.51

5 Discussion

Quality of life is evaluated by questionnaires that might be generic. The quality of life is determined by questionnaires, which can be generic, i. general or specific, taking into account the specificities of the particular illness. The most commonly used generic questionnaires are SF-6 and EQ-5D. The SF-36 (Item Short Form) contains 36 items and scales focusing on physical and mental health and physical activity limitations due to physical health problems, restrictions on social activities due to physical health and emotional problems, limitations on the execution of routine activities as a result of physical problems, physical pain and overall perception of health [12]. The EQ-5D is a standardized generic health assessment tool that evaluates two indicators - objective and subjective. Objectively include five items - mobility, self-healing, common activities, pain/discomfort, anxiety/depression [13].

Of the specific questionnaires used in thyroidology, the most used are: ThyPro, THYCA-QoL and GO-QoL. ThyPro is a questionnaire focusing on benign thyroid disease [14], THYCA-QoL is a questionnaire on malignant thyroid disorders [15] and GO-QoL is a questionnaire for patients with Graves ophthalmopathy [16].

The FZ TnUAD questionnaire consists of individual modules, respectively. parts of: - demographic, - clinical patient, - clinical, - quality of life, - socio-economic, - specific (eg symptom-focused) or comparative (other recognized questionnaire, whether specific or generic) Most items are designed to reflect the answers in numerical terms (eg from 0 - worst to 10 - the best, or some items have been adapted from conceptual scaling to a scale of 1 to 5). This approach allows for adequate statistical processing with subsequent validated evaluation of the results. The questionnaire also provides a retrospective evaluation of QoL and WA, while almost all other questionnaires evaluate only the current status or status for the last specified portion of life: usually the last 10-14 days. Virtually no available study was designed for retrospective assessment of quality of life by patients alone. This time, several studies overcame the comparison of the established quality of life with the quality of life in the ordinary population. In the case of primary hypothyroidism, the quality of life was lower than the normal population [17], and the same finding was found in the quality of life of patients with Graves hyperthyroidism as well as overall vitality compared to the general population [18,19]. The compensation status may not be in line with a full quality of life adjustment. Also, in patients with well-treated and well-compensated hypothyroidism, the quality of life was worse in all the parameters of quality of life, physical functioning, vitality, social functioning, mental health as well as in people without thyroid disorder, and was worse than in patients with euthyroid [20]. In this context, it can be stated that if we consider the quality of life of the disease-free life of the patients in our study as the equivalent in the population sample, our results are consistent with the outputs of all three.

The contribution of treatment to the quality of life in case of latent hypothyroidism was also discussed. While Razvi's work has confirmed this benefit in the case of l-thyroxine treatment [21]), this effect was not observed for latent hypothyroidism in patients over 65 years of age [22]. We did not follow the category of latent hypothyroidism in our work, so we can not comment on our findings from the point of view of our results.

Improvement in quality of life may not occur in part of the patient even with compensated hypothyroidism, as demonstrated by a Dutch study of 1667 patients who also had poor quality of life during treatment, as well as

reduced activity during the day [23]. This fact documents the need for an individual approach to treatment in patients who have documented good results, but they do not feel it subjectively.

There was a lot of work on the relationship of laboratory compensation and quality of life. No effects on quality of life in patients treated for primary hypothyroidism had either thyroid hormones or thyroid antibodies [17]. Similar results were obtained in a large study of 9,491 patients: HRQoL in the TSH suppressive group or significantly elevated TSH had no significant difference compared to the group of patients with normal resp. slightly elevated TSH significant difference, although HRQoL was lower than the group [24].

Thyroid technology has also examined the effect of thyroid gland surgery on quality of life. Quality of life improved after strumectomy (total or unilateral lobectomy), both in the group of patients with autoimmune thyroid gland and in the patient group with increased, non-autoimmune

[25]. In the case of Graves hyperthyroidism, there was no difference in the quality of life in relation to its solution, whether it was medical suppression, radiotherapy or surgical treatment [18]. On the overall quality of life, or on the physical or psychological area (or some of its characteristics) and their domains. Our work in its own way brings a broad spectrum of monitored parameters and their correlation to the quality of life. The limitation of the work is an unqualified questionnaire although some of the other quality-oriented questionnaires used were not validated, as well as the number of patients with hyperthyroidism and after strumectomy, which may have an effect on the results.

6 Conclusions

The quality of life differs significantly at the time of diagnosis and then in treatment like hypothyroidism (Thyrozol, Propycil) have no significant effect on the quality of life in the treatment of hyperthyroidism. Bladder (Euthyrox, L-Thyroxine BCH) have no significant effect on the quality of life at the time of diagnosis. The quality of life in patients with total strumectomy or unilateral lobectomy does not differ from patients with hypothyroidism and hyperthyroidism. Positive family, work, economic and health expectations, higher education and positive personality base correlate with the quality of life in hypothyroidism. medical care positively correlates with QoL in hyperthyroidism as well as hypothyroidism There was no correlation with marital status, duration of the disease, duration of the symptoms before diagnosis, the number of endocrinologist visits, knowledgeability about the disease and willingness to pay, that the patient is hypothetically willing to pay for full recovery.

References

- [1] Podoba, J., Hnilica, P., Srbecký, M., Bednář, J. Thyroid volume, goitre and diff use lymphoid thyroiditis in adolescents after long-term iodine prophylaxis in Slovakia. *J Endocrinol. Invest.* 1992; 15 (S5): 14.
- [2] Amino, N., Tada, H., Hidaka, Y. Chronic (Hashimoto's) Thyroiditis. In: DeGroot, L.J., Jameson, J.L.(Eds): *Endocrinology*, 4th Edition, Philadelphia, London; WB Saunders Company. 2001: 1471–1480.
- [3] Weetman, A.P. Autoimmune Thyroid Disease. In: DeGroot, L.J., Jameson, J.L. (Eds): *Endocrinology*, 4th Edition, Philadelphia, London; WB Saunders Company 2001: 1409– 1421.
- [4] Gharib, H., Tuttle, R.M., Baskin, H.J., Fish, L.H., Singer, P.A., McDermott, M.T. Subclinical thyroid dysfunction: a joint statement on management from the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society. *Endocr Pract.* 2004; 10 (6): 497–501.
- [5] Fatourechi, V. Subclinical hypothyroidism: an update for primary care physicians. *Mayo Clin. Proc.* 2009; 84 (1): 65–71.
- [6] Villar, H.C., Saconato, H., Valente, O., Atallah, A.N., Villar, H.C, ed. Thyroid hormone replacement for subclinical hypothyroidism. *Cochrane Database Syst Rev.* 2007; (3): CD003419.
- [7] Burch, H.B., Cooper, D.S. Management of Graves Disease. *JAMA.* 2015; 314 (23). doi:10.1001/jama.2015.16535. ISSN 0098-7.
- [8] Stárka, L. et al. *Endokrinologie*. Triton, 2010, ISBN:978-80-7387-328-8, 231 s.
- [9] Torrance, G.W. Utility approach to measuring healthrelated quality of life. *J Chronic Dis.* 1987; 40 (6): 593–603.
- [10] Patrick, D.L. et al. Content Validity - Establishing and Reporting the Evidence in Newly Developed Patient-Reported Outcomes (PRO) Instruments for Medical Product Evaluation: ISPOR PRO Good Research Practices Task Force Report: Part 1 - Eliciting Concepts for a New PRO Instrument. *Value in Health*, 2001; 14 (8): 967-977.
- [11] Bielik, J., Ondrušová, A., Matisáková, I., Gerlichová, K., Poliaková, N., Mišinová, M. Nový koncept kvality života s prenosom do rokov života štandardizovanej kvality aplikovanej do liekovej. *Farmakoekonomika a lieková politika.* 2013; 9 (4): 14-17.
- [12] Ware, J.E.jr, Sherbourne, C.D. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992; 30 (6): 473-483.
- [13] Devlin, N.J., Brooks, R. EQ-5D and the EuroQol Group: Past, Present and Future. *Appl Health Econ Health Policy.* 2017; 15 (2): 127–137.

- [14] Watt, T. et al. Validity and reliability of the novel thyroid-specific quality of life questionnaire, ThyPRO. *European Journal of Endocrinology*. 2010; 162: 161–167.
- [15] Husson, O. et al. Development of a disease-specific health-related quality of life questionnaire (THYCA-QoL) for thyroid cancer survivors. *Acta Oncol*. 2013; 52 (2): 447-454.
- [16] Terwee, C.B. et al. Development of a disease specific quality of life questionnaire for patients with Graves' ophthalmopathy: the GO-QOL. *Br J Ophthalmol*. 1998; 82: 773-779.
- [17] Kelderman-Bolk, N. et al. Quality of life in patients with primary hypothyroidism related to BMI. *Eur J Endocrinol*. 2015; 173 (4): 507-515.
- [18] Abraham-Nordling, M. et al. Graves disease: a long-term quality-of-life follow up of patients randomized to treatment with antithyroid drugs, radioiodine, or surgery. *Thyroid*. 2005; 15 (11): 1279-1286.
- [19] Abraham-Nordling, M. et al. Thyroid hormone state and quality of life at long-term follow-up after randomized treatment of Graves disease. *Eur J Endocrinol*. 2007; 156 (2): 173-179.
- [20] Morgunova, T. et al: Quality of life in patients with hypothyroidism. *Clinical and experimental thyroidology*. 2010; 6 (2): 62-67.
- [21] Razvi, S. et al. The Beneficial Effect of L-Thyroxine on Cardiovascular Risk Factors, Endothelial Function, and Quality of Life in Subclinical Hypothyroidism: Randomized, Crossover Trial. *The Journal of Clinical Endocrinology & Metabolism*. 2007; 92 (5): 1715-1723.
- [22] Young, J.P. et al. Subclinical hypothyroidism (SCH) is not associated with metabolic derangement, cognitive impairment, depression or poor quality of life (QoL) in elderly subjects. *Archives of Gerontology and Geriatrics*. 2010; 50 (3): 68-73.
- [23] Mollewijk, E. et al. Reduced quality of life and persistent complaints in treated hypothyroid patients. *Endocrine Abstracts*. 2018; 56 GP274, DOI: 10.1530/endoabs.56.GP274.
- [24] Klaver, E.I. et al. Thyroid Hormone Status and Health-Related Quality of Life in the LifeLines Cohort Study. *Thyroid*. 2013; 23 (9): 1066–1073.
- [25] Zivaljevic, V.M. et al. Quality of life improvement in patients with Hashimoto thyroiditis and other goiters after surgery: A prospective cohort study. *International Journal of Surgery*. 2015; 21: 150-155.